Notice of Allowability	Application No.	Applicant(s)	
	10/802,574	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *5/9/05*.

2. ☒ The allowed claim(s) is/are *5,9,13,16,23,29,34,39 and 46*.

3. ☒ The drawings filed on *17 March 2004* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____.
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

1.00

DETAILED ACTION

Status of the Claims

1. Claims 2-3, 5-17, 19, 21-23, 25-40 and 42-54 are pending.

Applicants' amendment and response filed February 15 and May 9, 2005 are acknowledged. Applicant's response has been fully considered. Claims 5, 13, 16, 23, 34, 39 and 46 have been amended, and claims 1, 4, 18, 20, 24 and 41 have been cancelled. It appears the product claims as amended (claims 5, 16, 23 and 39) are free of prior art and allowable, thus, the method claims (claims 9, 13, 29, 34 and 46), which have the same scope as the product claims, are rejoined for examination. Claims 2, 3, 6-8, 10-12, 14, 15, 17, 19, 21, 22, 25-28, 30-33, 35-38, 40, 42-45 and 47-54 are non-elected inventions and are withdrawn from consideration. Therefore, claims 5, 9, 13, 16, 23, 29, 34, 39 and 46 are examined.

Withdrawn Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1, 4, 16, 20, 23 and 39 under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's amendment to the claims, applicants' cancellation of the claim, and applicant's response at page 8 in the amendment filed February 15, 2005.

3. The previous rejection of claims 1, 4, 5, 16, 18, 20, 23, 24, 39 and 41 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's amendment to the claims, applicants' cancellation of the claim, and applicant's response at page 8 in the amendment filed February 15, 2005.

Withdrawn Claim Rejections - 35 USC § 102

4. The previous rejection of claims 20 and 23 under 35 U.S.C. 102(b) as being anticipated by Shone *et al.* (WO 95/33850), is withdrawn in view of applicant's amendment to the claims,

applicants' cancellation of the claim, and applicant's response at pages 8-9 in the amendment filed February 15, 2005.

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Sana Pratt on July 18, 2005.

Examiner's Amendment to the Specification:

-Please replace the paragraph at page 1, lines 5-6 with the following paragraph:

This application is a Continuation of U. S. Patent Application No. 09/962,360, filed September 25, 2001, now U. S. Patent 6,762,280, which claims benefit of U. S. Provisional Application No. 60/235,050, filed September 25, 2000.

-Please replace the term "**Figure 2**" with "**Figures 2a and 2b**" at page 7, line 17.

Examiner's Amendment to the Claims:

Cancel claim 2, 3, 6-8, 10-12, 14,15, 17, 19, 21, 22, 25-28, 30-33, 35-38, 40, 42-45 and 47-54.

Claims 5, 9, 13, 16, 23, 29, 34, 39 and 46 have been amended as follows:

5. (Currently amended) A botulinum neurotoxin serotype B or tetanus toxin substrate containing a fluorescent signal moiety on one side of the cleavage site that produces a fluorescent signal and a moiety that quenches the magnitude of said signal on the other side of the cleavage site such that when the substrate is cleaved, an increase in fluorescent signal is produced, ~~and~~ wherein said substrate is a peptide identified [in] as SEQ ID NO:3 or SEQ ID NO:4.

9. (Currently amended) A method for measuring the concentration of botulinum neurotoxin serotype B or tetanus neurotoxin in a sample, said method comprising:

mixing the sample with a peptide substrate ~~according to claim 1~~ identified as SEQ ID NO:3 or SEQ ID NO:4,

measuring an increase in fluorescent signal with time produced from proteolytic cleavage of said substrate, and[[,]]

determining the concentration of said neurotoxin by ~~correlation~~ correlating to a standard of said neurotoxin.

13. (Currently amended) A method for detecting the presence of botulinum neurotoxin serotype B or tetanus toxin proteolytic activity in a sample, said method comprising:

mixing the sample with ~~one or both~~ a peptide substrates identified ~~in~~ as SEQ ID NO:3 or SEQ ID NO:4, and

detecting an increase in fluorescent signal produced from proteolytic cleavage of said substrate.

16. (Currently amended) A kit for determining the concentration of botulinum neurotoxin serotype B or tetanus toxin in a sample, the kit containing in close confinement[[,]]:

(i) one or both peptide substrates according to claim 5 cleavable by said botulinum neurotoxin or said tetanus toxin; and

(ii) said botulinum neurotoxin standard or said tetanus toxin standard.

23. (Currently amended) A botulinum neurotoxin serotype B or a tetanus toxin substrate comprising a peptide ~~or protein~~ which ~~may be~~ is optionally immobilized to a solid material and which contains a fluorescent moiety that produces a measurable fluorescent signal such that when the substrate is cleaved, the fluorescent signal is released, ~~and~~ wherein said substrate is a peptide identified ~~in~~ as SEQ ID NO:9.

29. (Currently amended) A method for detecting the presence of ~~clostridial~~ botulinum neurotoxin serotype B or tetanus toxin proteolytic activity in a sample, said method comprising:

mixing the sample with a peptide substrate ~~according to claim 20~~ identified as SEQ ID NO:9, and

detecting an increase in fluorescent signal produced from proteolytic cleavage of said substrate.

34. (Currently amended) A method for measuring the concentration of botulinum neurotoxin serotype B or tetanus toxin in a sample, said method comprising:

mixing the sample with a peptide substrate identified ~~in~~ as SEQ ID NO:9,

measuring an increase in fluorescent signal with time produced from proteolytic cleavage of said substrate, and[[,]]

determining ~~an increase~~ the concentration of said neurotoxin by ~~correlation~~ correlating to a standard of said neurotoxin.

39. (Currently amended) A kit for determining the concentration of botulinum neurotoxin serotype B or tetanus toxin in a sample, the kit containing in close confinement[[,]]:

(i) the peptide substrate according to claim 23 cleavable by said botulinum neurotoxin or said tetanus toxin; and

(ii) said botulinum neurotoxin or said tetanus toxin standard.

46. (Currently amended) A method for identifying ~~inhibitors or enhancers of~~ a compound that inhibits or enhances the proteolytic activity of botulinum neurotoxin serotype B or tetanus neurotoxin, said method comprising:

preincubating the neurotoxin with a test compound to make a neurotoxin-compound solution,

exposing said solution to a peptide substrate identified ~~in~~ as SEQ ID NO:9,

measuring fluorescent signal resulting from ~~proteolysis~~ proteolytic cleavage of said substrate by said neurotoxin, and

comparing said fluorescent signal of the neurotoxin-compound solution with a control[[s]],

wherein the control is the neurotoxin solution without the presence of the test compound, and wherein an increase in fluorescent signal indicates a compound ~~which~~ that enhances neurotoxin activity and a decrease in fluorescent signal indicates a compound ~~which~~ that inhibits said neurotoxin.

The following is an **Examiner's Statement of Reasons for Allowance**: The following reference appears to be the closest art to the claimed invention. Soleilhac *et al.* (Anal. Biochem. 241, 120-127 (1996)) teach a fluorescent peptide substrate [Pya^{88}] S 39-88 for tetanus toxin. However, the reference does not teach or suggest a FRET peptide substrate of SEQ ID NO:3 or SEQ ID NO:4, and a fluorescent peptide substrate of SEQ ID NO:9 for botulinum toxin B and tetanus toxin. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. CMK
Patent Examiner

CMK
July 18, 2005

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER